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Effects of Cigarette Smoking Upon Dogs

I. Design of Experiment; Mortality; Findings in Lung Parenchyma.

by

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In numerous epidemiologic and histologic studies, it has been found that the ill effects of cigarette smoking increase with the number of cigarettes smoked per day. This points to a dose-response relationship. The dose of tar and nicotine delivered in the smoke from a cigarette can be reduced in any of several ways, one way being the use of a filter. Thus it might be supposed that if tar and nicotine are mainly responsible for the ill effects, then smoking cigarettes equipped with an efficient filter may be less harmful than smoking the same number of identical cigarettes not so equipped. The present experiment was conducted to test this hypothesis and to determine whether cigarette smoking would eventually lead to lung cancer in dogs.

In a preliminary experiment, ten beagle dogs smoked cigarettes daily by means of a tube inserted in a tracheostoma. ^{7.8)} Five of the dogs died within the first 415 days of smoking, one death being due to bronchopneumonia and the other four to pulmonary infarction due to emboli. In three of these cases the emboli apparently came from a thrombus in the right auricular appendage. The remaining five dogs were sacrificed on days 421 to 423 after having smoked 3,700 to 4,100 non-filter cigarettes of a brand which was reported to be high in tar and nicotine. At autopsy, all of the sacrificed dogs were

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filter-tip cigarettes for a longer length of time would have eventually resulted in severe damage to the lung parenchyma.

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In planning this experiment we hypothesized that under these conditions greater biological damage would be produced by smoke with a high concentration of tar and nicotine than by smoke with half the concentration of tar and nicotine (total dosage being the same over a period of many months or years). One of our aims was to test this hypothesis. It was based upon the theory that high concentration would tend to overpower the defense mechanisms of the body and thereby lead to effectively higher dosage than a lower concentration. The principal physiological effects of nicotine depend upon the concentration of nicotine in the blood at a moment of time. Since nicotine is removed from the blood very rapidly, a high concentration in the blood can be

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achieved only by rapid delivery of nicotine into the blood. It would seem that nicotine would be delivered into the blood more rapidly from smoke with a large amount of nicotine than by the same volume of smoke with half that amount of nicotine. Most of the tar and nicotine in cigarette smoke is contained in particles. Particles are removed from the alveoli by alveolar phagocytes and are removed from the bronchial tubes and trachea in bronchial secretions propelled by ciliary action. Presumably, there is a limit to the rapidity with which the removal can take place even if the removal mechanisms are undamaged. Thus it seems likely that a higher concentration of particles occur on lung surfaces if particulate matter is delivered rapidly (concentrated smoke) than if delivered less rapidly (less concentrated smoke). In addition, cigarette smoke retards ciliary action and, in sufficient concentration, can lead to ciliastasis. (Certain of the ciliastatic agents are in the gases⁹⁾ rather than in the particles contained in cigarette smoke).

In order to test this hypothesis, we attempted to find filter-tip cigarettes such that the filter produced a 50% reduction in both tar and nicotine. We could not find such cigarettes. The filters in the cigarettes used effected a 49% reduction in tar but only a 37% reduction in nicotine. During a period of 875 days, group F dogs which smoked filter-tip cigarettes received 6% more tar and 29% more nicotine than group L dogs which smoked non-filter cigarettes. (See table 1). Nevertheless, histopathologic changes in the lung parenchyma were somewhat less extensive in group F dogs (filter-tip) than in group L dogs (non-filter). This finding is consistent with the hypothesis.

Findings in relation to the occurrence of tumors will be described in the second of this series of papers.

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